In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

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MICHAEL MAGER, as parent of VICTORIA MAGER,	*	
	*	No. 14-820V
	*	Special Master Christian J. Moran
Petitioner,	*	
v.	*	Filed: July 29, 2021
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Entitlement; human papillomavirus ("HPV") vaccine; autoimmune epilepsy; sudden unexpected death in epilepsy ("SUDEP"); diagnosis.
Respondent.	*	
* *		

Renee J. Gentry, Vaccine Injury Clinic, George Washington University Law School, Washington, DC, for petitioner;
Laurie Wiesner, United States Dep't of Justice, Washington, DC, for respondent.

DECISION DENYING COMPENSATION[1]

Michael Mager alleges that the human papillomavirus ("HPV") vaccine his deceased daughter Victoria received on September 11, 2012, caused her to suffer autoimmune epilepsy leading to sudden unexpected death in epilepsy. He seeks compensation pursuant to the National Childhood Vaccine Injury Compensation Program.

As detailed below, the undersigned finds that Mr. Mager is not entitled to compensation because based on the evidence submitted, he has not met his burden

[1] The E-Government Act, 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services), requires that the Court post this decision on its website. This posting will make the decision available to anyone with the internet. Pursuant to Vaccine Rule 18(b), the parties have 14 days to file a motion proposing redaction of medical information or other information described in 42 U.S.C. § 300aa-12(d)(4). Any redactions ordered by the special master will appear in the document posted on the website.

to show that Victoria suffered from autoimmune epilepsy. Furthermore, because this is a threshold issue for which the evidence and briefing already submitted is sufficient to make a determination, a hearing is not required.

I. Procedural History

Represented by attorney Mark Krueger, Mr. Mager asserted that the HPV vaccination Victoria received on October 2, 2007, caused her to suffer a seizure disorder leading to her death on January 11, 2014. Pet., filed Sept. 5, 2014, at Preamble, ¶ 12. Mr. Mager filed an amended petition on November 19, 2014. He then gathered medical records, including those requested by the Secretary in advance of the Rule 4(c) report, and the record was complete on February 17, 2015.

The Secretary filed his Rule 4(c) report on April 1, 2015, contesting causation and arguing that Victoria's seizure disorder existed pre-vaccination. Resp't's Rep. at 8-11. Mr. Krueger withdrew from the case on May 18, 2016. Mr. Mager submitted a fact witness affidavit on July 7, 2015. Ms. Renee Gentry was substituted as counsel of record for Mr. Mager on August 3, 2016, after which the case proceeded to the expert report stage. After multiple extensions, Mr. Mager filed his first expert report from Dr. Mikovits and Dr. Ruscetti on November 17, 2016.[2] The Secretary then filed responsive expert reports from Dr. Fujinami and Dr. Kohrman on March 2, 2017, and March 22, 2017, followed by supplemental expert reports from Mr. Mager on May 25, 2017; October 12, 2017; and October 27, 2017. The Secretary submitted supplemental expert reports on March 19, 2018, and Mr. Mager submitted his final supplemental expert reports on May 25, 2018.

In a status conference held on June 19, 2018, the undersigned discussed the relative weaknesses of Mr. Mager's expert reports and his attorney requested additional time to retain a pediatric neurologist to better support his claim. Mr. Mager then filed an expert report from Dr. Shafrir on October 3, 2018. In this report, Dr. Shafrir raised the potential helpfulness of obtaining the slides from Victoria Mager's autopsy. While Mr. Mager began the process of attempting to obtain the autopsy slides and the exchange of expert reports continued, the case was referred to alternative dispute resolution ("ADR") on January 30, 2019. However, the parties failed to reach a settlement agreement and the case was

[2] Because Mr. Mager eventually chose not to rely on the opinions of Dr. Mikovits or Dr. Ruscetti, all submissions from these expert witnesses were later stricken from the record.

removed from ADR on March 25, 2019. Respondent then filed supplemental expert reports on April 22, 2019.

Dr. Shafrir asserted a diagnosis of autoimmune epilepsy based, in part, on what he deemed neurological reactions to the vaccine that suggested underlying autoimmune encephalitis. Exhibit 55 at 18. Dr. Kohrman, however, maintained a diagnosis of juvenile myoclonic epilepsy ("JME"), based on his view that Victoria suffered pre-vaccination seizure activity, non-focal (i.e. generalized) seizures, and a lack of evidence regarding an autoimmune process in Victoria's autopsy. Exhibit Y at 7. Dr. Fujinami agreed with the JME diagnosis, highlighting that Victoria's seizures were not treatment resistant, as would be true of seizure activity involved in autoimmune epilepsy. Exhibit CC at 1-2. Dr. Shafrir and Dr. Kohrman both have significant experience in neurology and pediatric neurology, exhibit 56; exhibit B, though Dr. Kohrman has particularly strong experience regarding epilepsy and pediatric epilepsy, including a current board certification with the American Board of Psychiatry and Neurology with a subspecialty in epilepsy. Exhibit B at 2. Dr. Fujinami has significant experience as an immunologist. Exhibit J.

After trying for an extended period to obtain the autopsy slides, Mr. Mager filed a status report on October 28, 2019, stating that a supplemental expert report from Dr. Shafrir would not be necessary. The undersigned issued an order for submissions in advance of potential adjudication on November 20, 2019. After multiple extensions, Mr. Mager filed a supplemental expert report from Dr. Shafrir on July 25, 2020, and his brief on July 27, 2020. The Secretary, again after multiple extensions, filed his supplemental expert reports from Dr. Fujinami and Dr. Kohrman, as well as his brief, on February 10, 2021. Mr. Mager filed his reply brief on March 26, 2021. With the briefing complete, this case is ripe for review.

II. Standards for Adjudication

Petitioners are required to establish their cases by a preponderance of the evidence. 42 U.S.C. § 300aa–13(1)(a). The preponderance of the evidence standard requires a "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010) (citations omitted).

To receive compensation, petitioners must establish five elements. 42 U.S.C. § 300aa–11(c)(1)(A) through (E); 42 U.S.C. § 300aa–13(a)(1)(A) (authorizing special masters to award compensation when petitioners establish

items listed in section 11(c)(1)). To establish causation for off-Table injuries, petitioners bear a burden "to show by preponderant evidence that the vaccination brought about [the vaccinee's] injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Althen v. Sec'y of Health & Human Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005).

The process for finding facts in the Vaccine Program begins with analyzing the medical records, which are required to be filed with the petition. 42 U.S.C. § 300aa–11(c)(2). Medical records that are created contemporaneously with the events they describe are presumed to be accurate. Cucuras v. Sec'y of Health & Human Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993).

Furthermore, as a threshold matter, a petitioner must establish she suffers from the condition for which she seeks compensation. Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d 1339, 1346 (Fed. Cir. 2010). When a petitioner fails to establish her diagnosis, there is no need for an analysis pursuant to Althen v. Sec'y of Health & Human Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005). Lombardi v. Sec'y of Health & Human Servs., 656 F.3d 1343, 1353 (Fed. Cir. 2011).

III. Diagnostic Criteria

Mr. Mager alleges that Victoria Mager suffered from autoimmune epilepsy. However, the Secretary contends that her condition was more likely indicative of JME. See exhibit A at 13-14. The difference between autoimmune epilepsy and JME affects the outcome of Mr. Mager's case because his theory of causation relies on an autoimmune disease causing neuroinflammation. To better assess whether Mr. Mager has met his burden in establishing that Victoria suffered from autoimmune epilepsy, as well as the Secretary's assertion of JME as the more likely diagnosis, it is necessary to set forth the diagnostic criteria for each.

A. Autoimmune Epilepsy

The three major indicators of autoimmune epilepsy are: (1) "demonstration of autoantibodies against neuronal components in the patient's blood"; (2) in most patients, seizures that "may not respond to regular antiepileptic medications but respond to immunomodulatory treatment"; and (3) "occurring in relation to an autoimmune disease or autoimmune encephalitis." Pet'r's Br. at 9-10.[3] With

[3] Mr. Mager states that he gleaned these diagnostic criteria from exhibit 88 and exhibit 65 and that this specific list "does not appear" verbatim in the medical literature filed. Pet'r's Status

respect to the third criterion, Mr. Mager alleges that Victoria suffered from autoimmune encephalitis. The diagnostic indicators of autoimmune encephalitis include:

> (1) Focal seizures, particularly focal motor and focal dyscognitive, secondary generalized seizures; (2) seizure clusters, status epilepticus; (3) seizures and epilepsy of unknown cause; (4) refractory seizures; (5) associated features of encephalopathy, movement disorders, neuropsychiatric symptoms, cognitive or memory impairment; and (6) history of autoimmune diseases (personal or family).

Exhibit 65 (Suleiman) at 3.[4] Focal seizures are those in which the onset in the brain is localized, while the onset of generalized seizures is not localized. Secondary generalized seizures start out localized, but then spread to both sides of the brain. Refractory are those which do not respond to anti-seizure medications. As outlined above, focal, secondary generalized, and/or refractory seizures are clinical indicators specific to autoimmune encephalitis, though both focal/secondary generalized and primary generalized seizures can occur in people with autoimmune encephalitis. Thus, while presence of a focal, secondary generalized, and/or refractory seizure would necessarily indicate autoimmune encephalitis, presence of a primary generalized seizure could indicate autoimmune encephalitis or juvenile myoclonic epilepsy because primary generalized seizures occur with both conditions. Mr. Mager points out that "it is not necessary to find each of these attributes to come to a diagnosis of autoimmune encephalitis," id. (citing exhibit 65), "origin of seizure onset is difficult to determine with certainty," id. at 12 (citing exhibit BB (Dr. Kohrman's report), tab 4, at 1), and autoimmune epilepsy can occur in patients with milder presentations, see Pet'r's Br. at 10 (citing exhibit 88).

B. Juvenile Myoclonic Epilepsy

In his brief, the Secretary sets out the clinical features of JME as: (1) presence of myoclonic, tonic-clonic, and/or absence seizures; (2) an average onset age of 15.1 years, although this metric is highly variable; and (3) myoclonic seizures may precede the first generalized tonic-clonic seizure by 6-12 months, although generalized tonic-clonic seizures occur as the first seizure type in

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Rep., filed June 17, 2021, CM/ECF No. 188. Respondent did not challenge this list as the criteria for autoimmune epilepsy in any of his briefs. Therefore, the undersigned will accept these criteria for the purposes of this decision.

[4] For a more detailed analysis of the Suleiman article, see Moriarty v. Sec'y of Health & Human Servs., No. 03-2876V, 2016 WL 5390172, at *28 (Fed. Cl. Spec. Mstr. Aug. 23, 2016), vacated and remanded, 130 Fed. Cl. 573 (2017).

approximately one third of patients. Resp't's Br. at 13-14 (citing exhibit BB (Dr. Kohrman's report)). Unlike autoimmune epilepsy, JME produces seizures that generally respond to anti-seizure medication and is characterized by the presence of primary generalized, not focal or secondary generalized, seizures. See id. at 14 (citing exhibit BB).

IV. Facts

Victoria Mager was born on July 29, 1995. Pet. ¶ 1. Prior to receiving the vaccination that is the subject of Mr. Mager's claim on her behalf, Victoria suffered from enuresis, or bed wetting, at approximately eight years old. Exhibit 18 at 5. Her primary care provider also noted that she was receiving speech therapy at this time and experienced "poor performance" and "decreased attention" at school during this time. Id. Other than this, Victoria's pre-vaccination health history appears relatively normal.

On September 4, 2007, Victoria received the meningococcal and tetanus-diphtheria-acellular pertussis ("Tdap") vaccines. Exhibit 4 at 2, 3. She then received the HPV vaccine on October 2, 2007. Id. at 2, 9. On November 14, 2007, Victoria experienced a seizure and was taken to the emergency room of Children's Hospital of Wisconsin. Exhibit 11 at 28. In her admission notes, the description of her condition states that she experienced a seizure followed by a second seizure approximately four minutes later. Id. A head CT scan, urine toxicology screen, and chest x-ray were performed with normal results. Id. at 3-4, 13. An EEG was then performed, the results of which were "[i]ntermittent epileptiform spike & low wave discharges over the left frontal region, as well as the bifrontal region, maximal on left" and "intermittent generalized spike and slow wave discharges, maximum over left frontal region, seen predominantly during drowsiness and sleep." Id. at 17. It was noted that these discharges "indicate focal sites of cerebral hyperexcitability which can be associated with partial seizures/epilepsy." Id. Victoria was prescribed Depakote, an anti-seizure medication, and discharged on November 15, 2007. Id. at 38.

On December 12, 2007, Victoria saw a pediatric neurologist, Dr. Sharif, for a follow-up. Dr. Sharif noted that, after she was discharged, her parents recalled and reported to Dr. Sharif in this appointment that "for a while, [Victoria] was waking up with big cuts in her tongue at least twice and also complaining of soreness after waking up and it is possible that these might have been seizures." Exhibit 11 at 75. Victoria's stepmother also reported that there had been no more bed wetting incidents after the prescription of Depakote between her hospital admission and this appointment. Id. Dr. Sharif noted an impression of "focal

onset epilepsy by EEG" and "some frontal lobe dysfunction." Id. at 77. Dr. Sharif recommended neuropsychological testing. Id.

Victoria saw another pediatric neurologist, Dr. Koehn, approximately two months later on February 21, 2008. An EEG was performed, the results of which were normal. Exhibit 6 at 22. Referring to the original abnormal EEG taken during her hospital admission, Dr. Koehn noted that "[t]he first EEG pattern could represent a fragment/a more lateralized pattern of an underlying generalized discharge or it could in fact be a focal discharge. Therefore, leaving the possibility open for this to have been a primary or secondarily generalized seizure." Id. at 20. Victoria's father and stepmother requested that she be weaned off Depakote, although the medication appeared to be controlling her seizure activity. They cited poor performance and difficulties focusing in school, which they thought may have been attributable to the Depakote. Id. at 24. Dr. Koehn therefore directed that she be gradually weaned off Depakote and referred her for neuropsychological testing. Id. at 28; see also Pet. ¶ 4.

On April 1, 2008, Victoria underwent neuropsychological testing with Dr. Waltonen. Exhibit 6 at 6. Dr. Waltonen noted that she had "a history of some type of learning difficulty at least in the speech and language area." Id. at 6. He also noted a family history of epilepsy and seizures on her maternal side. Id. at 2. With respect to learning and school-related difficulties, he noted that Victoria's stepmother reported "increasing problems with doing well in school" and Victoria's teachers indicated "problems following directions." Id. at 1, 4. Dr. Waltonen ultimately concluded that "[o]verall, her examination does not reveal evidence of significant cognitive impairment with the exception of very focal language findings." Id. at 6. He further recommended that "her language be looked at a bit more extensively" and, under "Plan," noted "Refer to the school for speech and language evaluation." Id. at 6-7.

Between April 2008 and her next medical event in October 2012, Victoria appears to have been functioning normally. School records submitted from part of this time period do not indicate any abnormalities. See exhibit 83. She received a normal sports physicals and health maintenance exams on August 8, 2009, and March 2, 2012. Exhibit 10 at 15-17; exhibit 14 at 1-2. She also saw Dr. Budde for a physical exam and removal of hand warts on January 5, 2012, when she reported that she had not experienced seizure activity in four years. Exhibit 10 at 18. On September 11, 2012, she received her second HPV vaccination. Exhibit 4 at 1. Approximately one month later, she was taken to the emergency department of Theda Clark Medical Center on October 10, 2012, after suffering a seizure. Exhibit 7 at 9. Her work-up, including an EKG, was normal. Id. at 13-14. She was diagnosed with a "probable seizure" and discharged. Id. at 14.

She saw her primary care doctor, Dr. Budde, on November 8, 2012. Exhibit 9 at 39. At this appointment, she reported two additional seizures following her ER visit on October 19, 2012, and November 7, 2012. Id. Dr. Budde prescribed Depakote and referred her to a neurologist. Id.

Victoria saw neurologist Dr. Edgar on January 14, 2013. Exhibit 9 at 24-25. An EEG was also performed. Dr. Edgar noted that the "EEG is normal during wakefulness. During sleep there is activation of infrequent potentially epileptiform activity over the left frontal and bioccipital head regions, consistent with the patient's history of generalized seizures." Id. at 25. Dr. Edgar's impression was primary generalized seizure disorder and he noted "age of onset at approximately 11 years of age suggests the possibility of juvenile myoclonic epilepsy, although no myoclonic seizures are reported." Id. at 9. He recommended Depakote but, after Victoria specified that she did not wish to remain on Depakote, Dr. Edgar directed her to begin weaning off Depakote and prescribed Keppra, a different anti-seizure medication. Id. at 8.

During a follow-up appointment with Dr. Edgar on July 8, 2013, he stated that Victoria's compliance with her Keppra prescription had been "less than ideal," with a sub-therapeutic level of the medication in her blood documented from a test on May 30, 2013. Exhibit 9 at 3. Victoria expressed a desire to discontinue use of Keppra, but Dr. Edgar persuaded her to remain on the drug given her history of seizures. Id. at 4. Dr. Edgar noted "probable juvenile myoclonic epilepsy" at this appointment due to age of onset. Id.

On January 11, 2014, Victoria was rushed to the emergency department after being discovered unresponsive at a friend's house. Exhibit 8 at 2. She was pronounced dead upon her arrival at the ER. Id. As part of an investigation of the death by the Waukesha Police Department, a witness reported that Victoria had been "missing a lot of doses of her medication" and Mr. Mager reported that "she was having seizures more frequently." Exhibit 13 at 2.

An autopsy was performed by Dr. Okia on January 13, 2014. Exhibit 12 at 1. The findings included pulmonary edema and brain changes consistent with a seizure disorder. Exhibit 16 at 1. Sections of the brain showed focal areas of subpial gliosis. Id. at 6. Furthermore, a toxicology screen showed levels of Keppra in her blood. Exhibit 13 at 11. According to the toxicology report, regular dosing of Keppra results in 3-37 mcg/mL in the blood, with peak levels of 10-60 mcg/mL within 1.5 hours after dosage. Id. Victoria's toxicology results revealed 26 mcg/mL of Keppra in her blood at the time of death. Id. Victoria's death certificate listed "seizure disorder" as her cause of death. Exhibit 1 at 1.

V. Analysis

This section will first analyze the relative qualifications of the experts, specifically Dr. Shafrir and Dr. Kohrman, as their expertise is relevant to their diverging opinions regarding Victoria's diagnosis. Next, this section will consider whether Mr. Mager has met his burden to prove each diagnostic criterion for autoimmune epilepsy: presence of autoimmune antibodies, response to anti-seizure medications, and co-existing autoimmune disorder. Because in order to satisfy the third criterion, Mr. Mager asserts that Victoria suffered from autoimmune encephalitis, section B. includes an analysis of whether he has met his burden to show each of the six diagnostic criteria for autoimmune encephalitis. Finally, section C. discusses statements from treating doctors.

A. Qualifications of Experts

Because a determination regarding whether Mr. Mager has met his burden to prove Victoria suffered from autoimmune epilepsy hinges in part on the diagnostic opinions of Dr. Shafrir and Dr. Kohrman, it is helpful to compare their qualifications as a preliminary matter. Special masters may consider the relative expertise of testifying experts when weighing the value of their opinion. See Depena v. Sec'y of Health & Human Servs., No. 13-675V, 2017 WL 1075101 (Fed. Cl. Spec. Mstr. Feb. 22, 2017), mot. for rev. denied, 133 Fed. Cl. 535, 547-48 (2017), aff'd without op., 730 Fed. App'x 938 (Fed. Cir. 2018); Copenhaver v. Sec'y of Health & Human Servs., No. 13-1002V, 2016 WL 3456436 (Fed. Cl. Spec. Mstr. May 31, 2016), mot. for rev. denied, 129 Fed. Cl. 176 (2016).

Though both Dr. Shafrir and Dr. Kohrman have ample experience and expertise in pediatric neurology, Dr. Kohrman has a notable special expertise in epilepsy. For example, Dr. Kohrman holds a current board certification with the American Board of Psychiatry and Neurology with a subspecialty in epilepsy. Exhibit B at 2. Dr. Shafrir's board certifications include pediatrics, neurology, and psychiatry with a special qualification in child neurology, and clinical neurophysiology. Exhibit 56 at 2. Both experts have published in the areas of epilepsy and pediatric epilepsy. However, Dr. Kohrman's publication history specific to issues involving pediatric epilepsy appears more extensive. See exhibit B at 3-9; exhibit 56 at 4-6. Though Dr. Shafrir's certifications and topics of focus in his publications are certainly relevant and helpful to this case, Dr. Kohrman's specialty in epilepsy—particularly his board certification with a subspecialty in epilepsy and focus on pediatric epilepsy—makes him particularly qualified to opine on a case in which potential diagnoses of autoimmune epilepsy or juvenile myoclonic epilepsy are at play.

B. Diagnosis of Autoimmune Epilepsy

The three major indicators of autoimmune epilepsy are: (1) "demonstration of autoantibodies against neuronal components in the patient's blood"; (2) in most patients, seizures that "may not respond to regular antiepileptic medications but respond to immunomodulatory treatment"; and (3) "occurring in relation to an autoimmune disease or autoimmune encephalitis." Pet'r's Br. at 9-10. Each of these indicators will be addressed in turn.

1. Presence of autoimmune antibodies

Mr. Mager concedes, based on Dr. Shafrir's report that, with the respect to the first element of autoimmune epilepsy, Victoria was not tested for autoimmune antibodies in her blood. Exhibit 85 at 4. Thus, there is no affirmative evidence on this point. Mr. Mager asserts potentially valid reasons why Victoria's treating doctors may not have thought to perform tests relevant to an autoimmune epilepsy diagnosis. Specifically, he asserts that autoimmune epilepsy is a relatively "emerging field." Pet'r's Reply at 18. He refers vaguely to comments made by both his and respondent's experts. However, it is unclear where these assertions regarding the emerging nature of this diagnosis are located in any of the reports. Still, even assuming this is true and that there is a valid reason for the lack of testing, a *lack* of evidence on this point does not help Mr. Mager's case. While this fact is not dispositive as to the determination of whether Victoria had autoimmune epilepsy, and does not rule out autoimmune epilepsy, a lack of testing also does not provide any affirmative evidence supporting an autoimmune epilepsy diagnosis.

Mr. Mager also concedes via Dr. Shafrir's report that no autoimmune process was detected from Victoria's autopsy. Exhibit 85 at 4. However, Dr. Shafrir in his first report pointed to the finding of gliosis in Victoria's autopsy as an indicator of an inflammatory process. Specifically, he stated:

> Gliosis is typically an inflammatory mechanism which is induced by various brain insults. Although we do not have a good description of the extent, cellular components, and the localization of the gliosis in the postmortem examination of Victoria's brain, it definitely supports an inflammatory mechanism as a cause of epilepsy.

Exhibit 55 at 20. He argues that this constitutes evidence of autoimmunity because of the connection between autoimmunity and inflammatory responses. Id. at 19-20. In response, Dr. Fujinami contended that gliosis found in Victoria's autopsy is a "common finding in epilepsy and represents the result of a neuronal injury and cell death . . . and not an acute or chronic inflammatory process related to

vaccination." Exhibit Y at 7. Mr. Mager states that medical literature relied upon by Dr. Fujinami contradicts this contention. In his reply brief, he states that astrogliosis, like that detected in Victoria's autopsy, can indicate inflammatory attacks. Pet'r's Reply at 19 (citing exhibit Y-15 at 8). Dr. Kohrman agrees that gliosis is a "regular finding in juvenile myoclonic epilepsy" and that the pathologist "concluded this was a typical finding in epilepsy and [Victoria] ha[d] primary generalized epilepsy." Exhibit BB at 15. Thus, the experts dispute the significance of the gliosis finding as it pertains to evidence of autoimmunity.

The connection made between the gliosis found in Victoria's autopsy and the potential for an inflammatory response, which may indicate autoimmunity is tenuous. While there may be some chance of an inflammatory process—and thus, in Dr. Shafrir's opinion, evidence of autoimmunity—indicated by the gliosis in Victoria's autopsy, this does not tip the scale persuasively in the direction of an autoimmune disease, as evidenced by the conclusions of the pathologist performing the exam. It also does not provide evidence of autoimmune antibodies in Victoria's blood, which is the actual relevant criterion in terms of testing for a diagnosis of autoimmune epilepsy.

2. Response to anti-seizure medications and refractory seizures

The second clinical feature of autoimmune epilepsy is seizures that do not respond to anti-seizure medication, also called refractory seizures. See Pet'r's Reply at 13-14. As detailed in the facts, Victoria was prescribed Depakote after her first emergency room visit in November 2007 and weaned off the medication at her father's request starting in February 2008. She was then prescribed Keppra, another seizure medication, in November 2012 after her second emergency room visit for a seizure. She maintained the Keppra prescription until her death in January 2014.

To support the contention that Victoria's seizures were resistant to anti-seizure medication, Mr. Mager points to two particular incidents: (1) Victoria suffered a seizure the night she was discharged from the hospital in November 2007, after she had been prescribed and started on Depakote; and (2) levels commensurate with prescriptive use of Keppra were found in her blood upon her death.

To the first point, while Mr. Mager did report that Victoria experienced a seizure after being discharged from the hospital, there is also evidence that, after she began taking Depakote, her seizure-related activity, such as enuresis, stopped. Exhibit 11 at 75 (report by stepmother in December 2007 appointment with Dr.

Sharif). Her providers, including Dr. Sharif and Dr. Koehn, recommended continuation of Depakote. At her appointment with Dr. Koehn in February 2008, she had a normal EEG and no reports of seizure activity since the night of her hospital discharge. Exhibit 6 at 20. Victoria's parents requested that she be weaned off Depakote, however, against Dr. Koehn's recommendations, see id. at 20-21 (noting a discussion of potential recurrent seizures if not on Depakote and recommending Keppra if seizures recur), and Victoria did not take Depakote or experience seizure activity between approximately February 2008 and October 2012 when she began to experience her second bout of seizure activity. Thus, the single seizure occurring the night of her hospital discharge after she had just begun taking Depakote does not outweigh the months of a lack of seizure activity while on Depakote, that was further supported by a normal EEG and recommendations to continue anti-seizure medication at her appointment with Dr. Koehn in late February 2008.

To the second point, regarding presence of Keppra in her blood upon death, Victoria was prescribed Keppra after her seizure and hospitalization in October 2012, as an alternative to Depakote. However, multiple medical records discuss Victoria's irregular use or lack of adherence to her Keppra prescription. After Dr. Edgar initially prescribed Keppra in January 2013, Victoria returned to him for a follow-up in July 2013. In this appointment, Dr. Edgar noted that Victoria's compliance with her Keppra prescription had been "less than ideal," with a sub-therapeutic level of the medication in her blood documented from a test on May 30, 2013. Exhibit 9 at 3. Based on the notes from this visit, it also appears that Victoria was generally averse to continuing her Keppra prescription, perhaps because of unwanted side effects. Id. at 4. However, Dr. Edgar persuaded her to continue with the medication in light of potential recurrent seizure activity. Though there were what appear from the toxicology report to be levels of Keppra detected in Victoria's blood during her autopsy that were consistent with the range present as a result of normal dosing, a source noted that Victoria had been "missing a lot of doses of her medication" and Mr. Mager reported that "she was having seizures more frequently" leading up to her fatal seizure in January 2014. Exhibit 13 at 2. Thus, multiple sources of evidence show that Victoria did not take Keppra as prescribed and was having seizures leading up to her death. Because of this, the contention that levels of Keppra in her blood at death shows the presence of refractory seizures is unpersuasive, given the evidence against regular adherence to anti-seizure medication. There is no other evidence, besides these two instances which appear unpersuasive, that Victoria's seizures were resistant to anti-seizure medications. In fact, there is some contradictory evidence from the few months when she was taking Depakote as prescribed, that this anti-seizure medication was effective in controlling her seizure activity.

3. Association with autoimmune encephalitis

The third and final clinical indicator of autoimmune epilepsy is association with an autoimmune disease. To this point, Mr. Mager specifically asserts that Victoria suffered concurrently from autoimmune encephalitis. The diagnostic criteria for autoimmune encephalitis are:

> (1) Focal seizures, particularly focal motor and focal dyscognitive, secondary generalized seizures; (2) seizure clusters, status epilepticus; (3) seizures and epilepsy of unknown cause; (4) refractory seizures; (5) associated features of encephalopathy, movement disorders, neuropsychiatric symptoms, cognitive or memory impairment; and (6) history of autoimmune diseases (personal or family).

Pet'r's Reply at 11 (citing exhibit 65). According to Mr. Mager, "It is not necessary to find each of these attributes to come to a diagnosis of autoimmune encephalitis, but 'the suspicion of autoimmune encephalitis should be predominantly based upon clinical characteristics and supportive investigations.'" Pet'r's Reply at 11 (quoting exhibit 65 at 1).

i. Focal vs. Generalized Seizures

Focal seizures, or seizures which begin in a localized part of the brain, are clinical indicators of autoimmune encephalitis. Exhibit 65 (Suleiman) at 1. Secondary generalized seizures, or seizures that start out localized and then spread to both sides of the brain, are also included as clinical indicators of autoimmune encephalitis. Id. Generalized seizures, which do not have a localized onset, however, can occur in people with autoimmune encephalitis or juvenile myoclonic epilepsy.

Victoria's EEG results indicated that her seizures were not focal or secondary generalized. To counteract this lack of evidence, Mr. Mager argues, citing respondent's medical literature, that "EEGs of patients suffering from autoimmune epilepsy 'may have variable findings including normal, focal, and generalized slow activity, periodic discharges, and focal epileptiform discharges.'" Id. at 12 (quoting exhibit BB, tab 4, at 1). Additionally, "in a study of children with new-onset epilepsy, over 40% of these children experienced generalized seizures." Id. at 16 (citing exhibit 65). However, Dr. Kohrman states that "generalized discharges are the hallmark of [primary or idiopathic generalized epilepsies]." Exhibit BB at 2-3.

Though the classification of Victoria's seizures as generalized does not rule out autoimmune encephalitis, it also does not constitute affirmative evidence of

autoimmune encephalitis. In other words, the presence of generalized seizures could indicate *either* autoimmune encephalitis or juvenile myoclonic epilepsy, whereas only the presence of focal or secondary generalized seizures would point specifically to a diagnosis of autoimmune epilepsy. After factoring in Dr. Kohrman's comment that generalized seizures are also the "hallmark" of primary or idiopathic generalized epilepsies (i.e. epilepsies without an autoimmune component), as well as the fact that Dr. Kohrman possesses superior expertise with respect to epilepsy, see supra Part V.A, this makes Mr. Mager's argument even less persuasive.

ii. Seizure Clusters, Status Epilepticus

Mr. Mager states that Victoria *may* have suffered *one* seizure cluster, referring to her first hospital admission in November 2007. Pet'r's Reply at 12-13. Specifically, he states that, after her ER visit, which was precipitated by a seizure, "she suffered a three-minute seizure followed very closely by a shorter seizure, without recovering between the two." Id. at 13 (citing exhibit 6 at 24). It is not clear whether "status epilepticus" was applicable to this particular "cluster." However, it also does not appear that "status epilepticus" is necessarily present in a case of autoimmune encephalitis. Id. (citing exhibit 65 at 4). Still, while this incident following Victoria's November 2007 hospitalization could constitute a seizure cluster, it also does not provide persuasive evidence regarding this particular indicator of autoimmune encephalitis, or evidence of autoimmune encephalitis as a whole, given the inconclusiveness of a classification of this incident as a "cluster" and the fact that, if it was, it was an isolated incident.

iii. Seizures of Unknown Cause

It does appear that treaters in this case were not uniform in their assessment of the cause of her seizures. During her first hospitalization, it was noted that the discharges detected in her EEG "indicate focal sites of cerebral hyperexcitability which can be associated with partial seizures/epilepsy." Exhibit 4 at 17. At her second hospitalization, the reason for her visit was noted as "probable seizure." Exhibit 7 at 14. Dr. Sharif noted an impression of "focal onset epilepsy by EEG." Exhibit 11 at 77. Dr. Koehn, in her assessment, elected to "leave[] the possibility open for this to have been a primary or secondarily generalized seizure." Exhibit 6 at 20. Finally, Dr. Edgar diagnosed her with "probable juvenile myoclonic epilepsy" based on age of onset. Exhibit 9 at 4. Thus, this clinical factor does appear to be present in Victoria's case in that no treater gave her a certain diagnosis or cause of her seizures and there is some disagreement on ultimate conclusions among treaters. However, because this factor represents a lack of information by definition, rather than information pointing specifically to a

diagnosis of autoimmune encephalitis, it appears to be a less persuasive indicator than some of the other factors discussed.

iv. Refractory Seizures

As explained above, see supra Part V.B.2, Mr. Mager has not met his burden to show that Victoria's seizures were refractory, or in other words resistant to anti-seizure medication.

v. Movement Disorders, Neuropsychiatric Symptoms, and/or Cognitive or Memory Impairment

Mr. Mager asserts that Victoria experienced cognitive impairment and bases this assertion on neuropsychological testing performed by Dr. Waltonen in April 2008. Pet'r's Reply at 14-15. Dr. Waltonen ultimately concluded that "overall, her examination does not reveal evidence of significant cognitive impairment with the exception of very focal language findings." Exhibit 6 at 6. In his brief, Mr. Mager emphasizes the language findings as proof that the results of this testing were irregular. However, Victoria has a documented history of "some type of learning difficulty at least in the speech and language area." Id.; see also exhibit 18 at 5 (pre-vaccination notation from a primary care provider regarding "poor performance" and "decreased attention" at school). It does not appear that the results of Dr. Waltonen's assessment, which were very narrowly limited to language-related deficits, can rise to the level of a cognitive impairment indicative of autoimmune encephalitis, especially when these language issues existed to some degree long before her vaccination. See exhibit A at 12 (Dr. Kohrman opining that Victoria's normal range IQ "argues against a neurodegenerative disorder as a cause for the seizures").

vi. History of Autoimmune Diseases

Mr. Mager concedes that Victoria did not have any significant personal or family history of autoimmune disease. Pet'r's Reply at 15. While, as Mr. Mager points out and as is true with the other diagnostic indicators of autoimmune encephalitis, this fact is not dispositive, the absence of a family or personal history of autoimmune disease further adds to the lack of persuasiveness with respect to the existence of autoimmune encephalitis.

vii. Summary: Autoimmune Encephalitis

Thus, with respect to autoimmune encephalitis, the only diagnostic criterion that Mr. Mager has met his burden to show is that Victoria's seizures were of an unknown cause. It follows that Mr. Mager has then not met his burden in showing

that Victoria suffered from autoimmune encephalitis, as this is only one of six diagnostic criteria, and one that is relatively less weighty given that it by definition indicates a *lack* of information regarding Victoria's condition.

C. Lack of Support from Treating Doctors

The opinions of treating doctors regarding the diagnosis of a petitioner's condition are generally favored given that, having examined the petitioner, they are in the best position to opine on the petitioner's condition. See Capizzano v. Sec'y of Health & Human Servs., 440 F.3d 1317, 1326 (Fed. Cir. 2006). In this case, no treating doctors diagnosed Victoria with autoimmune epilepsy.

On December 12, 2007, pediatric neurologist Dr. Sharif noted an impression of "focal onset epilepsy by EEG." Exhibit 11 at 77. On February 21, 2008, pediatric neurologist Dr. Koehn assessed her abnormal EEG during her hospitalization as indicating a possible "primary or secondarily generalized seizure," but did not diagnose her with any specific type of epilepsy. Exhibit 6 at 20.

Later, she was assessed with "probable seizure" during her hospitalization in October 2012, exhibit 4 at 14, and subsequently visited her primary care doctor who prescribed anti-seizure medication, exhibit 9 at 39. Again, no diagnoses of epilepsy were made. On January 14, 2013, neurologist Dr. Edgar noted an impression of primary generalized seizure disorder and stated: "age of onset at approximately 11 years of age suggests possibility of juvenile myoclonic epilepsy." Exhibit 9 at 9. Dr. Edgar again noted "probable juvenile myoclonic epilepsy" at a second appointment on July 8, 2013. Id. at 4.

Thus, as evidenced by these records, none of Victoria's treating doctors diagnosed her with autoimmune epilepsy, or in fact made a definitive diagnosis at all. The closest Victoria came to receiving a diagnosis were Dr. Edgar's impressions. However, Dr. Edgar specifically stated that he suspected probable juvenile myoclonic epilepsy, not autoimmune epilepsy. The lack of support from treating doctors regarding a diagnosis of autoimmune epilepsy is yet another factor that weighs against finding that Victoria suffered from autoimmune epilepsy.

D. Conclusion: Autoimmune Epilepsy

As explained above, Mr. Mager advanced the presence of autoimmune encephalitis as an associated autoimmune disease as one of three overall diagnostic indicators of the asserted diagnosis—autoimmune epilepsy. Mr. Mager has not met his burden to show either the presence of autoimmune antibodies in Victoria's blood or that Victoria's seizures were refractory. See supra Parts V.B.1, V.B.2.

Because he also could not persuasively show that Victoria suffered from autoimmune encephalitis, and therefore an associated autoimmune disease, see supra Part V.B.3, it follows that he has not shown by a preponderance of the evidence that Victoria suffered from autoimmune epilepsy. Because he has not established the threshold issue of diagnosis, it also follows that further analysis regarding causation is unnecessary. See Lombardi v. Sec'y of Health & Human Servs., 656 F.3d 1343, 1353 (Fed. Cir. 2011); Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d 1339, 1346 (Fed. Cir. 2010).

If an Althen analysis were performed, then one element is that Mr. Mager establish, by preponderant evidence, "a proximate temporal relationship between vaccination and injury." Althen, 418 F.3d at 1278. Here, relying upon a post-marketing study, Slade, Mr. Mager asserts that a window of 4-42 days was "'biologically plausible.'" Pet'r's Br. at 45, quoting exhibit 59 (Slade) at 5.

Mr. Mager further maintains that Victoria developed seizures within the appropriate time. In 2007, she received her first dose of the HPV vaccine on October 2, 2007. Exhibit 4 at 2, 9. She suffered a seizure on November 14, 2007. Exhibit 11 at 3. The interval between these events is 43 days.

Five years later, Victoria received a second dose of the HPV vaccine on September 11, 2012. She then experienced a seizure on October 10, 2012. The interval between these events is 29 days.

In response, the Secretary does not strenuously argue that the seizures occurred outside an expected window. Instead, the Secretary points out that "temporal proximity alone is insufficient to establish causation." Resp't's Br. at 23, citing Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1323 (Fed. Cir. 2010) and Grant v. Sec'y of Health & Human Servs., 956 F.2d 1144, 1148 (Fed. Cir. 1992).

The sequence of events in Victoria's life in that she twice experienced seizures after receiving the HPV vaccine seems to underlie Mr. Mager's good faith belief that the vaccinations harmed his daughter and, ultimately, caused her death much too soon. However, Congress has not allowed special masters to award compensation based upon a petitioner's belief alone. 42 U.S.C. § 300aa–13(a)(1); see Shyface v. Sec'y of Health & Human Servs., 165 F.3d 1344, 1349 (Fed. Cir. 1999). Although Mr. Mager has present opinions from a qualified expert, Dr. Shafrir, his opinion that Victoria suffered autoimmune epilepsy is not persuasive for the reasons explained at length above. And, without this predicate showing, examination of Dr. Shafrir's opinions regarding all Althen prongs is not required according to Federal Circuit precedent.

VI. Ruling on the Record is Appropriate

Special masters may rely on accumulated knowledge in the Vaccine Program to make entitlement decisions on the papers. Thus, special masters, "based upon their accumulated expertise in the field, judg[e] the merits of individual claims." Whitecotton v. Sec'y of Health & Human Servs., 81 F.3d 1099, 1104 (Fed. Cir. 1996) (quoting Hodges v. Sec'y of Health & Human Servs., 9 F.3d 958, 961 (Fed. Cir. 1993)). Additionally, special masters retain wide discretion in determining whether an evidentiary hearing is necessary. Kreizenbeck v. Sec'y of Health & Human Servs., 945 F.3d 1362, 1365 (Fed. Cir. 2020) (citing 42 U.S.C. § 300aa-12(d)(3)(B)(v) ("In conducting a proceeding on a petition a special master . . . may conduct such hearings as may be reasonable and necessary.")). The special master must only determine "that the record is comprehensive and fully developed before ruling on the record." Id. at 1366 (citing Simanski v. Sec'y of Health & Human Servs., 671 F.3d 1368, 1385 (Fed. Cir. 2012)).

A hearing to determine the threshold issue of diagnosis in this case is not needed. The parties have had ample opportunity to develop their positions through submissions of evidence (primarily medical records) about Victoria, lengthy and multiple expert reports, and thorough briefing.

Mr. Mager's claim fails for reasons that a hearing could not cure given the paucity of evidence establishing a diagnosis of autoimmune epilepsy, which is essential for the remainder of Mr. Mager's claim to proceed. He has had a full and fair opportunity to present his case. Thus, a disposition on the papers is appropriate. See Kreizenbeck, 945 F.3d at 1365.

VII. Conclusion

For the foregoing reasons, the undersigned finds that Mr. Mager has not met his burden to show, by a preponderance of the evidence, that Victoria suffered from autoimmune epilepsy. Therefore, Mr. Mager has not shown that the HPV vaccination caused her to suffer autoimmune epilepsy resulting in sudden unexpected death in epilepsy. Accordingly, the claim for compensation is DENIED.

The Clerk's Office is instructed to enter judgment in accord with this decision unless a motion for review is filed. Information about the submission for a motion for review, including deadlines, is presented in the Vaccine Rules, which are available through the Court's website.

IT IS SO ORDERED.

s/Christian J. Moran
Christian J. Moran
Special Master

Appendix of Articles Cited

Barbara A. Slade et al., *Postlicensure Safety Surveillance for Quadrivalent Human Papillomavirus Recombinant Vaccine*, 302 J. Am. Med. Ass'n 750 (2009), filed as exhibit 59.

Jehan Suleiman et al., *The recognition and treatment of autoimmune epilepsy in children*, 57 Dev. Med. & Child Neurology 431 (2015), filed as exhibit 65.

Jehan Suleiman et al., *Autoantibodies to neuronal antigens in children with new-onset seizures classified according to the revised ILAE organization of seizures and epilepsies*, 54 Epilepsia 2091 (2013), filed as exhibit 88.

Alexei Verkhratsky & Arthur Butt, *General Pathophysiology of Neuroglia*, in Glial Physiology and Pathophysiology 431 (2013), filed as exhibit Y, tab 15.